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09/349,954	07/08/1999	NICHOLAS KIM HAYWARD	10441Z	7397

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SCULLY SCOTT MURPHY & PRESSER
400 GARDEN CITY PLAZA
GARDEN CITY, NY 11530

EXAMINER	
SAOUD, CHRISTINE J	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/349,954	Applicant(s) HAYWARD et al.
	Examiner Christine Saoud	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 25, 2002* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *26-28, 30, and 46-58* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *26-28, 30, 46-49, and 56-58* is/are allowed.

6) ☒ Claim(s) *50-55* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Claims 50-54 have been amended as requested in the amendment of paper #20, filed 25 June 2002. Claims 26-28, 30 and 46-58 are pending in the instant application.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed 25 June 2002 have been fully considered but they are not deemed to be persuasive.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 50-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

7. Claims 50-55 are not enabled for making a "biologically active VEGF-B" by using a nucleic acid molecule with hybridizes under high stringency conditions for the reasons of record in paper #18. These claims are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making biologically active VEGF-B by expressing a nucleic acid molecule of SEQ ID NO:3, 5, 7 or 9, does not reasonably provide enablement for expressing a nucleic acid molecule which hybridizes under high stringency conditions to said nucleic acid molecules of SEQ ID NO:3, 5, 7 or 9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant argues that "given the high stringency conditions described and claimed, only a vey limited number of sequences would hybridize". This argument is not persuasive because, the claims encompass any nucleic acid which hybride and would make "biologically active VEGF-B". The claims encompass small pieces of DNA, since these would hybridize, encompasses DNA which has mutations which would alter the coding sequence which could also hybridize, encompasses DNA which may encode other VEGF molecules other than the recited "VEGF-B", etc. However, the instant claims are not enabled for this breadth because it is not predictable which of those nucleic acid molecules which hybridize to the nucleic acid sequences of SEQ ID NO:3, 5, 7 or 9 will also encode a biologically active VEGF-B. It would require undue experimentation to practice the current invention because one of ordinary skill in the art would

not know which of those nucleic acid molecules that hybridize would also encode a polypeptide, which could be considered "VEGF-B" until the polynucleotide is expressed in a host cell, the protein produced and tested. Therefore, the instant claims are a wish to know, and do not meet the requirements of enablement.

Applicant asserts that Example 2 of the specification provides "explicit teachings" and provides a "road map for the identification of biologically active VEGF-B". This assertion is not persuasive because Example 2 merely points out the nucleotide sequence of the encoding molecule and database homology information, such as the conservation of 8 cysteines (common to the VEGF family). However, this information is not sufficient for determining whether a DNA which hybridizes to the claimed sequence encodes a biologically active VEGF-B polypeptide. All VEGF proteins share sequence homology as well as conservation of cysteine residues (generally 8, however, there may be a member of the protein family which only has 7 of the 8 cysteines). Additionally, all the members of the VEGF family seem to stimulate vascular endothelial cells, therefore, how would the skilled artisan know if the nucleic acid which hybridizes and encodes a VEGF protein, which may or may not be active, is a "VEGF-B" protein? Merely hybridizing under the recited conditions does not provide sufficient structure for defining a "biologically active VEGF-B". The claims fail to recite sufficient structural elements to provide for the necessary function in that the structure of hybridizing to the sequence of SEQ ID NO:3, 5, 7 or 9 is not sufficient for encoding a biologically active VEGF-B, therefore, the claims are not enabled. See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. Appls, and Interf. 1986) and *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

The instant fact pattern is directly analogous in that what is claimed are nucleic acid molecules that have yet to be isolated or characterized for the activity recited in the application and thereby constitutes a "wish to know" rather than a reduction to practice, absent evidence to the contrary. The decisions of *In re Fisher*, Amgen Inc. v. Chugai, and *In re Wands* are relied upon in the instant rejection (see below) and by the court in a recent CAFC decision, Genentech, Inc. V. Novo Nordisk, 42 USPQ2d, 100 (CAFC 1997) because they show that the judicial interpretation of the first paragraph of 35 U.S.C. § 112 requires that the breadth of the claims must be based upon the predictability of the claimed subject matter and no on some standard of trial and error. To argue that one can make material embodiments of the invention and then test for those that work in the manner disclosed or that the instant claims only encompass the working embodiments is judicially unsound. Unless one has a reasonable expectation that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are more likely to work than not without actually making and testing them, then the instant application does not support the breadth of the claims.

The issue is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. This position is consistent with the decisions in *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) and Amgen Inc. v. Chugai Pharmaceuticals Co. Ltd., 13 USPQ2d, 1737 (1990) and In re Wands, 8 USPQ2d, 1400 (CAFC 1988). The factors to be considered in determining whether a disclosure would require undue experimentation

include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims.

Due to the large quantity of experimentation necessary to generate the large number of molecules by the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art, and the breadth of the claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of which of those molecules which meet the structural limitations of the claims would also meet the functional limitations of the claims. It is this additional characterization and inventive contribution that is required in order to obtain the functional and structural data needed to permit one to practice the claimed invention that constitutes undue experimentation.

Double Patenting

8. Applicant's terminal disclaimer filed 25 June 2002 is proper and has been entered into the instant application. The double patenting rejection is withdrawn.

Allowable Subject Matter

9. Claims 26-28, 30, 46-49, 56-58 are allowable over the prior art of record.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Christine J. Saoud, Ph.D., whose telephone number is (703) 305-7519. The Examiner can normally be reached on Monday to Thursday from 8AM to 2PM. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. §§ 1.6(d) and 1.8). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternate number. Official papers filed After Final rejection filed by fax should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud